

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 427 WO		FOR FURTHER ACTION		See Form PCT/PEA/416
International application No. PCT/DK2004/000186		International filing date (day/month/year) 18.03.2004	Priority date (day/month/year) 21.03.2003	
International Patent Classification (IPC) or national classification and IPC A61K31/381, A61K31/27, C07C271/28, C07D333/02, C07D213/02, A61P25/00				
Applicant H. LUNDBECK A/S et al.				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand 21.09.2004		Date of completion of this report 15.02.2005		
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Bedel, C Telephone No. +49 89 2399-2506		



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/DK2004/000186

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

147 as originally filed

Claims, Numbers

1-36 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
- * If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

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PCT/DK2004/000186

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 1-3, 6-27 (partly), 30-36

because:

- ☒ the said international application, or the said claims Nos. 30-36 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

- ☒ the claims, or said claims Nos. 1-3, 6-27 (partly) are so inadequately supported by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for the said claims Nos. 1-3, 6-27 (partly)

- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

- ☐ has not been furnished

- ☐ does not comply with the standard

the computer readable form

- ☐ has not been furnished

- ☐ does not comply with the standard

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- ☐ See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT
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International application No.
PCT/DK2004/000186

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	7,8,10,13-17,20,26-28,30
	No: Claims	1-6,9,11,12,18,19,21,25,29,31-36
Inventive step (IS)	Yes: Claims	7,8,10,13-17,20,26-28,30
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-29
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/DK2004/000186

The present application concerns a substituted p-diaminobenzene derivative of formula (I) and its use as a potassium channel opener.

The search has been restricted to what appeared to be fully disclosed and supported in the present application, namely the compounds of formula (I) where the position in ortho of the amido group is always substituted (the possibility of no substitution on this position exists in claim 1 as presently drafted).

Documents D1-D7 all disclose compounds which fall within the scope of the compound claims, thereby destroying the novelty of these claims (see detail in search report).

D7 in particular disclose compounds without any substitution on the ortho position, which are used in the treatment of CNS disorders.

D8 which is the closest prior art, discloses analogs of retigabine and their use as potassium channel openers. These analogs however differ from the presently claimed compounds by the fact that the ortho position is substituted by an amino group (as in retigabine compound), while in the presently claimed compounds, this ortho position is one of the variable parts of the molecule and does not comprise any amino group directly linked to the phenyl ring.

The intended purpose of the application is to find alternative compounds to the compounds of D8, that can be used as potassium channel openers.

This technical problem has been apparently solved by the applicant by providing the compounds of formula (I).

Nothing in the prior art could have hinted the skilled person to that solution since according to D8 and D9 the amino group in ortho position seems to be an essential feature.

The other documents that disclose the substituted compounds do not disclose any effect on potassium channels nor on CNS disorders.